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United States Department of Agriculture

Animal and Plant Health Inspection Service

Program Aid 1582

Keeping America Free From Foreign Animal Diseases

Vesicular Diseases

GPO Depository Library Program

Volume 7

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This binder contains an integrated suite of educational materials about foot-and-mouth disease, vesicular stomatitis, swine vesicular disease, and vesicular exanthema of swine. The package can be used in a formal training setting, where a presenter will show the video tapes and narrate the slide show using this black-and-white brochure as the script. Or the materials can be used in a self-study program with the reader progressing at his or her own pace.

Within this brochure, readers will notice that certain paragraphs are preceded by a number. These numbers correlate to the slide set. The vesicular diseases slides are all marked "V" at the top of each plastic slide frame and are numbered sequentially from 1 to 159.

If you remove the slides from their protective clear-plastic sleeve (for example, to put them into a carousel for group viewing), please be sure to reposition them in the correct numeric order for the benefit of future users.

This shrink-wrapped suite includes two video tapes on foot-and-mouth disease, a slide set on all four vesicular diseases, and the brochure you are reading now. If your package is incomplete, please contact the following office for replacement materials:

U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Veterinary Services, Emergency Programs
4700 River Road, Unit 41
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Program Aid 1576 African Horse Sickness
Program Aid 1577 African Swine Fever
Program Aid 1578 Contagious Bovine Pleuropneumonia
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Issued April 1997

1 Vesicular Diseases

2 There are four vesicular diseases of domestic livestock:

- Foot-and-mouth disease (FMD)
- Vesicular stomatitis (VS)
- Swine vesicular disease (SVD)
- Vesicular exanthema of swine (VES)

These four diseases will be considered in the tutorial on FMD because the lesion they have in common is a vesicle. Laboratory assistance is required for a differential diagnosis.

3 Foot-and-Mouth Disease

Definition

4 FMD is a highly contagious viral infection primarily of cloven-hoofed domestic and wild animals. The disease is caused by an apthovirus and characterized by vesicles, with subsequent erosions in the mouth and sometimes also in the nares, muzzle, feet, or teats.

Etiology

5 FMD virus (FMDV) is a member of the genus *Apthovirus* in the family Picornaviridae. The virion is a small (23-nm) single-stranded RNA virus.

6 Electron photomicrograph of FMDV.

There are seven serotypes of FMDV: A, O, C, Asia 1, and Southern African Territories (SAT) 1, 2 and 3. Within these serotypes, more than 60 subtypes have been described, and new subtypes occasionally arise spontaneously. At any given time, however, there are only a few subtypes causing disease throughout areas where FMD is endemic. The importance of subtypes is that an FMD vaccine may have to be tailored to the subtype present in the area in which the vaccine is to be used.

7 Slide illustrating FMD serotypes.

FMDV is pH sensitive: the virion is inactivated when exposed to pH below 6.5 or above 11. However, in milk and milk products, the virion is protected and can survive temperatures at 70 °C for 15 seconds and a pH of 4.6.

FMDV will survive drying and can be carried on inanimate objects. The virus can survive for long periods in bone marrow and lymph nodes.

Effective Disinfectants

- Acetic acid (2 percent)
- Sodium carbonate (4 percent)
- Sodium hydroxide (2 percent)
- Iodophore disinfectants
- Chlorine dioxide disinfectants

History

8

In 350 B.C., Aristotle mentioned a cattle plague that could have been FMD or rinderpest.

In 1546, the Italian physician Fracastorius gave the first clear description of the disease. For the next 2 centuries, the number of outbreaks in Europe increased.

In 1897, Foeffler and Frosch demonstrated for the first time that FMD was caused by a filterable agent.

Before the availability of an FMD vaccine, when an outbreak of the disease occurred, European farmers would deliberately spread it to other animals in the herd by rubbing the tongues of infected cattle with a rough towel and then rubbing the same towel on the tongues of healthy cattle. Farmers did this to shorten the course of the disease in their herds and provide immunity against the next outbreak of FMD.

But observers noted that animals that recovered were not always protected against future outbreaks of FMD. This observation led to the demonstration in 1922 of type O (Oise Valley) and type A (Allemagne) in France. In 1926, a third serotype was recognized and named C in anticipation that the previously recognized serotypes would be renamed to allow naming of additional serotypes, A, B, C, etc. The SAT subtypes were described between 1934 and 1948, and Asia 1 was isolated in Pakistan in 1954.

Host Range

9

FMD primarily affects cloven-footed domestic and wild animals. Other susceptible species include hedgehogs, nutria, rats, armadillos, elephants, capybaras, and mice.

Geographic Distribution

10

After World War II, FMD had become widely distributed throughout the world. Today, the disease is endemic in Asia, Africa, and parts of South America. In South America, Chile has been free of FMD since 1955 and Uruguay since 1994. Argentina has not had an outbreak since April 1994.

Most European countries have been recognized as free of FMD. FMD vaccination is no longer practiced in countries belonging to the European Union. North and Central America, Australia, New Zealand, Japan, and the British Isles are free of FMD.

Geographic Serotype Prevalence of FMD

11 It is interesting that particular serotypes and subtypes of FMD tend to be restricted to certain areas of the world. Here are some examples:

Europe (historically)		A (5)	O (1)	C (1)	
Asia	Near East	A (22)	O (1)		
	Middle East	A (22)	O (1)	C	Asia (1)
	Far East	A	O (1)	C	Asia (1)
Africa	Central East to West	A			
	Northeast	O			
	Central and South	SAT 1 and 2			
	South	SAT 3			
	(Serotype C is uncommon in Africa.)				
South America		A (24), (27)	O (1)	C (3)	

Transmission

12 FMDV can be introduced into a free area in several ways:

- Direct or indirect contact with infected animals.
- Spread of aerosols from infected animals, given the proper humidity and temperature. Aerosols from bulk milk trucks spread FMD in England. A person in contact with infected animals may retain sufficient FMDV in his or her respiratory tract for 24 hours to serve as a source of infection for susceptible animals.
- Feeding of contaminated garbage (meat, milk, blood, glands, bones, cheese, etc.)

- Contact with contaminated objects (hands, footwear, clothing)

- Artificial insemination

13 Illustration of the duration of shedding of FMDV in semen. The red represents the presence of FMDV in semen and the yellow, the duration of clinical signs.

- Contaminated biologicals (e.g., hormones—extraction procedure may not inactivate the virus)

- Sabotage

Epidemiology

14 Once an animal becomes infected, the primary mode of spread is then via respiratory aerosols. Other important means of spread are direct and indirect contact.

In an outbreak of FMD, the three primary hosts transmit the disease as follows:

- Sheep act as maintenance hosts.

- Pigs act as amplifiers.

- Cattle act as indicators.

When sheep or goats become infected with FMDV, the disease may not be diagnosed for a considerable time because signs and lesions can be very mild. During this time, however, the animals will be producing infectious aerosols, contaminating fomites, and spreading the virus by contact. FMD in pigs spreads very rapidly because pigs produce 30 to 100 times as much virus in aerosols as do sheep or cattle. An infected pig can produce a hundred million infectious doses per day.

When cattle are infected with FMDV, signs and lesions usually develop more rapidly and are more severe than lesions in pigs, sheep, or goats. If cattle, sheep, and pigs are exposed together, cattle will usually get sick first. Possibly, cattle are subject to increased exposure due to their greater pulmonary tidal volume.

Some strains of FMDV seem to affect particular species more than other strains. For example, some strains affect pigs but not cattle. In South America, mature cattle have had clinical signs of FMD while sheep in an adjacent pasture were normal.

Incubation Period

15 In experimental exposure to FMDV, animals may develop signs of the disease within 12 hours, but the usual interval is 24 to 48 hours.

When susceptible animals are in contact with clinically infected animals (peak time of transmission is usually when vesicles rupture), clinical signs usually develop in 3 to 5 days.

Pigs fed infected garbage usually develop signs in 1 to 3 days. Intact oral epithelium is resistant to infection, but during the process of ingesting food, pigs may sustain injury, and FMDV may also enter through their tonsils.

Pathogenesis

16 Portals of entry of FMDV.

17 Sites of predilection for FMD lesions.

18 Portals of exit of FMDV.

The pathogenesis of FMD is believed to be

1. Inhalation or ingestion of the virus
2. Infection of cells in the nasal–pharyngeal area and lung
3. Replication of virus and spread to the local lymph nodes
4. Viremia
5. Infection of cells of most epithelial surfaces
6. Virus in body fluids and aerosol

7. Fever

8. Appearance of vesicles in the mouth, tongue, feet, and teats (areas of predilection because the epithelium in these areas is stressed). These lesions are usually accompanied by salivation, nasal discharge, dirty nose, and lameness.

9. Rupture of the vesicles and increased severity of the clinical signs

10. End of fever

11. End of viremia and presence of detectable antibody

12. Healing of lesions

13. Gradual decrease of virus in body fluids

14. Persistence of FMDV in esophageal–pharyngeal fluid:

- In cattle: 6–24 months
- In sheep: 4–6 months
- In pigs: Pigs do not become carriers.
- In Cape (African) buffalo: Lifelong carriers

The course of an FMD infection is 2 to 3 weeks. Secondary infection may delay recovery. A lactating animal may not recover to preinfection production because of damage to the secretory tissue.

Clinical Signs in Cattle

Initial signs include dullness, anorexia, fall in milk production, and fever of 103 to 105 °F (39.4 to 40.6 °C)

These signs are followed by excessive salivation (drooling), serous nasal discharge, and shaking or kicking of the feet or lameness.

Vesicles form, especially on the tongue, dental pad, gums, soft palate, nostrils, muzzle, interdigital space, coronary band, and teats.

After vesicle formation, salivation may be more marked, and nasal discharge and/or lameness may increase.

Pregnant cows may abort. Young calves may die without showing any clinical sign of FMD.

Gross Lesions in Cattle

The diagnostic lesions of FMD in cattle are single or multiple vesicles ranging in size from 2 mm to 10 cm. These lesions can occur at all sites of predilection.

On the Tongue—These usually progress in the following manner:

- A small blanched area develops in the epithelium.
- Fluid fills the area and a vesicle is formed.
- Vesicle enlarges and many coalesce with adjacent ones.
- Vesicle ruptures.
- Vesicular covering sloughs leaving an eroded (raw) area.
- A grey, fibrinous coating forms over the eroded area. This coating becomes yellow, brown, or green.
- Epithelium is restored, but the line of demarcation remains (line gradually fades).
- Occasionally “dry” FMD lesions develop.

Instead of vesiculating, the fluid is apparently lost as it forms, and the upper layers of the epithelium become necrotic and discolored. Then the lesion appears necrotic rather than vesicular.

On the Feet—The vesicle in the interdigital space is usually large due to movement and weight.

The lesion at the coronary band at first appears blanched; then there is separation of the skin and horn. When healing occurs, new horn is formed. But a line resulting from the coronitis is seen on the wall of the hoof.

Cardiac and Skeletal Lesions

Animals that die may have greyish or yellowish streaking in the myocardium—degeneration and necrosis; "tiger heart."

Skeletal muscle lesions occur but are rare.

22 Saliva drips from the mouth because of mouth lesions.

23 Same cow as in slide #22. Note the ring of saliva on the floor.

24 Tongue of the same cow 1 day after intradermal–lingual inoculation. The raised, round area in the center of the large, white, blanched area is the site of inoculation. The large, white blanched area is a vesicle. If this area is pressed, the upper layers of epithelium will move because they are detached from the deeper layers. This white, blanched tissue can be easily removed using forceps and a scissors and is an excellent specimen for confirming a diagnosis.

25 The tongue of the same cow 5 days after inoculation. Most of the white, blanched epithelium has sloughed off. There are still fragments of white, necrotic epithelium on the surface of the tip of the tongue.

26 Another tongue with three small, unruptured vesicles.

27 Tongue with a large ruptured vesicle—excellent specimen for diagnosis.

28 Tongue with "dry" FMD lesions.

29 Closeup of slide #28. Apparently after FMDV infection of the epithelium, the fluid leaks out and leaves areas of necrotic-appearing epithelium.

30 Ruptured vesicle in the gingiva of the dental pad. This sign could be confused with a traumatic injury. The tags of epithelium should be collected for a diagnostic specimen.

31 Ruptured vesicles and tags of epithelium on the dental pad and hard palate. Again, tags of epithelium should be collected.

32 Erosions on the dental pad. Note that the surfaces of the erosions are smooth. This is an older lesion; the infected epithelium has sloughed off, and the lesion is starting to heal. This is an undesirable lesion for collection of a diagnostic specimen.

33 A recently ruptured vesicle in the gingiva.

34 The rough, loose, easily removed epithelium in the medial canthus is a result of FMDV infection.

35 Blanching and vesicles along and above the coronary band of both claws. On the left claw, the swelling and vesicle are more evident. The fluid from the vesicle and the overlying epithelium would be excellent diagnostic specimens.

36 Blanching and vesicles along and above the coronary band of both claws. Note that the vesicles join over the interdigital space.

37 Blanching of the coronary and interdigital epithelium and a ruptured vesicle in the interdigital area.

38 Ruptured vesicles in the interdigital area.

39 Blanched epithelium—vesicle—on the end of the teat.

40 Ruptured vesicle on the end of the teat. This lesion most likely extends up the streak canal.

41 An eroded area on a pillar of the rumen. This is a common site for an FMDV lesion in the rumen.

42. The pale area in the myocardium of the ventricle is an area of myocardial necrosis. Look for pale or greyish streaks in the myocardium.

43 FMD in water buffalo. Note that, even at a distance, the drooling is easily observed.

44 Closeup of one of the animals in slide #43.

45 An erosion on the dental pad of a water buffalo.

46 An erosion on the dental pad of a water buffalo. This was the extent of the oral lesions.

47 **Sequelae to FMD in Cattle**

- Secondary infection—mouth, nose, feet
- Hoof deformation
- Low milk production
- Mastitis
- Unthriftiness—failure to gain weight (attributed to cardiac damage)
- Breeding problems
- Panting—associated with pituitary gland damage
- Diabetes mellitus

Microscopic Appearance of Epithelial Lesions in Cattle

The characteristic lesion of FMD is spongiosis. The cells in the stratum spinosum appear to lose their desmosomes, round up, and the area fills with fluid, allowing separation of the superficial and basal layers of the epithelium. There may be hemorrhage or a cellular infiltration into the vesicular area. When the upper layers of the epithelium are lost, the basal layer is still present, forming an erosion. Because of the intact basal layer, the lesion heals quite rapidly if there is no secondary infection.

48 Photomicrograph of an FMD vesicle. The area of the stratum spinosum is wide, and the cells in the stratum spinosum are rounded and detached from each other (spongiosis).

Clinical Signs of FMD in Swine

49 Initial signs are fever of 104 to 105 °F (40 to 40.6 °C), anorexia, reluctance to move, and a tendency to squeal when forced to move.

50 These signs are followed by

- Vesicles

  —on the coronary band and heels,

  —in the interdigital space (foot involvement is usually severe), and

  —on the snout.

- Mouth lesions (not too common). If they occur, they are smaller and of shorter duration than in cattle and tend to be a "dry" type lesion. There is no drooling.

- Sows may abort.

- Piglets may die without showing any clinical signs of FMD.

Series of Slides on Clinical Signs of FMD in Pigs

51 The position of this pig suggests sore feet. The pig does not want to stand on its front feet, and rear feet are positioned to minimize the weight on the claws. Pigs infected with FMDV will be reluctant to move, and when forced to move will squeal because their feet hurt.

The following slides on pig feet emphasize the extent of involvement in an FMD infection.

52 An early FMD lesion. There is blanching of the coronary band.

53 A more advanced lesion. The coronary band is white and swollen.

54 The area above the coronary band is swollen and hyperemic, and the coronary band is white. Note that the dewclaws have the same type of lesion.

55 The vesicle in the coronary band has ruptured, and the area above the coronary band has eroded.

56 The vesicles in the coronary band and above the heel have ruptured.

57 Because of trying to keep weight off its claws, it is common for a pig to have erosions of the skin over the rear of the tarsal areas and at the front of the carpal areas. These lesions probably result from a combination of stress on the epithelium and presence of FMDV in the lesion.

58 These are an older lesion. It has a dry surface.

59 Proliferation of tissue over old FMD lesions in the heels.

60 The black line in the area of coronary bands on the claw and dewclaws has resulted from a coronitis. In this case, the cause was an FMDV infection.

61 Another pig with a black line in the wall. As the wall grows, this black line will be pushed toward the end of the claw. When this line is seen on the wall, it means that there was a coronitis. When you see this sign on more than one foot, start thinking about a vesicular disease. At this stage, only serology can be helpful.

62 The whitish areas on the surface of the tongue are dry FMD lesions. Oral lesions are less frequent in pigs than in cattle, and when they do occur in a pig, the lesion is usually the dry type.

63 An erosion on the tip of the tongue; proximal to the eroded area is a blanched area of dead epithelium.

64 Dry-type FMD lesion on the buccal mucosa.

65 Vesicle on the dorsal part of the snout.

66 A large vesicle on the snout.

67 Ruptured vesicles on the snout.

68 Aspiration of fluid from a vesicle on the snout. Whenever an attempt is made to aspirate vesicular fluid, use a 20-gauge or smaller needle; insert the needle into normal epithelium adjacent to the vesicle and then move the needle so that the vesicle is penetrated through its bottom. If the needle penetrates the vesicle directly, there is much greater chance of the fluid being lost.

Clinical Signs of FMD in Sheep and Goats

69 Clinical signs tend to be very mild:

- Possible dullness
- Possible fever
- Possible small vesicles or erosions on the dental pad, lips, gums, tongue
- Mild lameness may be the only sign; possible vesicles or erosion on the coronary band or in the interdigital space
- Possible abortion
- Possible death of nursing lambs. In a recent outbreak in northern African, there was a high mortality in young lambs and goats.

Morbidity and Mortality

70 Morbidity (prevalence or incidence) is essentially 100 percent in a susceptible population.

Mortality (death rate) from FMD is usually less than 1 percent. But in young animals and/or animals with infection due to certain isolates, mortality can be high. In a recent outbreak in Israel, there was at least 50-percent mortality in wild mountain gazelles. The same virus caused typical low mortality

in cattle. A severe viral pancreatitis present in the gazelles accounted for the high mortality.

Field Diagnosis

71

In cattle, FMD should be considered whenever salivation and lameness occur simultaneously and/or a vesicular lesion is seen or suspected. Fever often precedes other clinical signs; therefore, febrile animals should be carefully examined. Early diagnostic lesions may be found before animals start to salivate, have a nasal discharge, or become lame. To avoid missing a diagnosis, examine the mouth of a lame animal and the feet of any animal with signs or lesions involving the mouth or nostrils. Anticipate that FMD will spread rapidly and there will be a high clinical attack rate. But recognize that there may be exceptions when a relatively avirulent strain appears or more resistant animals (e.g., sheep) are affected.

In pigs, sheep, and goats, FMD should be considered when animals have sore feet and/or a vesicular lesion is suspected.

Specimens for Laboratory Diagnosis

72

Because the various vesicular diseases have similar clinical signs, a laboratory diagnosis for FMD is mandatory. Oral, nasal, podal, or mammary lesions are good sources of specimens. The following should be collected from each of two or three animals:

1. Vesicular fluid—as much as possible

2. Epithelium covering a vesicle

3. Flaps of epithelial tissue still attached

For 2 and 3 above, try to collect about 0.5 g. Old necrotic or fibrinous material that is difficult to remove is undesirable and often is highly contaminated with bacteria.

4. About 5 mL of blood with anticoagulant. Viremia ends about 5 days after the onset of disease.

5. Esophageal–pharyngeal (OP) fluid from convalescent cattle, sheep, or goats—about 5 mL. This should be immediately diluted with an equal volume of cell culture fluid (e.g., Hanks balanced salt solution with lactalbumin hydrolysate) and shaken vigorously for about 1 minute. If the solution turns yellow (indicating a low pH, which could inactivate the virus), discard and collect another sample.

73

A probang in a cow. The edges on the cup of the probang are rounded; the purpose of the probang is to collect fluid from the esophagus. This fluid contains oral and pharyngeal secretions and cells, and secretions and cells that come up the trachea and are swallowed.

6. Blood for serum (10 mL of serum)

7. From dead animals, collect samples of epithelial lesions, lymph nodes, thyroid, adrenal gland, kidney, and heart (about 10 g).

8. Full set of tissues in formalin

If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quick-freeze the specimens and do not allow them to thaw during transit. If dry ice is used, be sure that the vials are tightly sealed with stopper and tape so that no carbon dioxide enters the vial. The carbon dioxide will lower the pH and inactivate FMDV. Epithelium can also be placed in buffered glycerin and kept at 39 °F (4 C°) or –4 °F (–20 °C). The ratio of epithelium to glycerin should not exceed 1:10.

74

Laboratory Diagnosis

Antigen Detection and Virus Isolation

In the laboratory, vesicular fluid and tissue homogenates are tested for antigen by the complement fixation (CF) test or the enzyme-linked immunosorbent assay (ELISA).

Vesicular fluid, tissue, blood, and OP fluid are used to inoculate cell cultures and animals.

Nucleic Acid Detection

Polymerase chain reaction (PCR).

To confirm the initial case of FMD, the virus **must** be isolated and identified.

Serology

The virus neutralization (VN) test in cell culture or serum protection test in baby mice is serotype specific. These tests can also be used to differentiate different subtypes within a serotype.

The agar gel immunodiffusion test for virus-infection-associated (VIA) antibody will detect antibody to all serotypes. It was originally believed that the VIA antibody resulted only from viral infection. However, it is now known that transient VIA antibody can develop after vaccination because there is a molecule of RNA polymerase (the VIA antigen) associated with each viral particle. VIA antibody is a very significant finding in nonvaccinated animals. In vaccinated animals, VIA antibody may mean that FMD virus is circulating in the population.

Control of FMD

75

The official attitude of a country regarding control of a disease depends on how seriously the disease affects the country, the financial and technical ability of the country, and what the country's neighbors are doing. The degree of control of FMD varies from

- Virtually no control in some Asian and African countries where FMD is enzootic, to
- Protection of valuable or accessible animals or vaccination along a border to provide a buffer zone (cattle may be vaccinated because of severity of the disease, but not sheep and goats), to
- Large-scale vaccination and quarantine with or without slaughter of infected animals, to
- Regulatory measures to prevent entry of FMDV and quarantine and an eradication program.

A country where FMD is endemic should be as concerned about the introduction of FMDV as a country that is free of FMD because the introduced virus may be a serotype to which native animals have no immunity.

76 The United States has remained free of FMD because it has prevented the introduction of FMDV by

- Controlling importation of livestock, zoological animals, and animal products;
- Controlling decontamination and disposal of garbage from international ships, aircraft, etc.;
- Maintaining a strong veterinary infrastructure; and
- Reporting and investigating all suspected vesicular diseases.

Experimentally it has been shown that FMDV will not be transmitted by bovine embryo transfer if the embryos have been processed by the technique recommended by the International Embryo Transfer Society and the Office of International Epizootics.

Vaccination

77 The first attempts to produce immunity to FMDV occurred when farmers would deliberately spread the disease to other animals in the herd by rubbing the tongues of healthy cattle with a rough towel contaminated with virus from the tongues of infected cattle. The cattle exposed to FMD by this technique developed the disease, and this shortened the disease course in the herd and often provided immunity against the next outbreak of FMD.

The use of FMD vaccine began in Europe about 1938. The vaccine was prepared from vesicular fluid and tongue epithelium from inoculated cattle. The virus was inactivated by formalin and heat, and aluminum hydroxide was added as an adjuvant.

78 Removing infected epithelium from the surface of bovine tongues for use in preparing an FMD vaccine.

About 1951, FMD vaccine was produced by the Frenkel method. Normal tongue epithelium was removed, minced, placed in a nutrient broth, and inoculated with FMDV. After replication of FMDV, the virus was inactivated with formalin and aluminum hydroxide was added as an adjuvant. This method and also virus propagation in cell culture are being used today to produce FMD vaccines.

79 Slicing epithelium off the surface of a normal bovine tongue for use in the Frenkel method of FMD vaccine production.

Outbreaks of FMD were traced to use of formalin-inactivated vaccine. Apparently, in some cases, vaccine contained viable virus. The inactivant of choice is acetylethelenimine. Today (1997), the classic FMD vaccines are prepared using binary ethyleneimine-inactivated virus and aluminum hydroxide–saponin or oil as an adjuvant. Double-emulsion oil vaccines have been shown to produce an immunity of longer duration than aluminum hydroxide–saponin vaccine, especially in pigs.

To date, molecular-engineered vaccines have not been as effective or as economical as the cell-culture vaccines.

When vaccinating animals, make sure that the vaccine contains the same subtype of virus as is in the area. Frequent checking of the serotype and subtype during an outbreak is necessary because FMDV frequently changes during natural passage through various species.

Protection induced by a good aluminum hydroxide vaccine decreases rapidly in 4 to 6 months. A double-emulsion oil vaccine can protect for up to 1 year.

Vaccinated animals that are not completely protected can be a source of infection. The virus may replicate in these animals and be shed, even though the animals do not show any clinical sign of infection.

80

Control or Eradication

The following steps are essential in an FMD control or eradication program:

- Stop movement of animals and animal products in the area affected.
- Slaughter infected animals (and known contact animals).
- Destroy carcasses.
- Disinfect vehicles leaving the infected area.
- Vaccinate. If eradication by slaughter fails, vaccination may be used to control the outbreak. Experimental results indicate that potent vaccine may induce sufficient immunity in 4 days to protect cattle exposed to FMD.
- Inform and educate the community.

81 Vesicular Stomatitis (VS)

82 Definition

VS—a viral disease caused by a *Vesiculovirus*—is characterized by fever, vesicles, and subsequent erosions in the mouth and epithelium on the teats and feet. Horses, cattle, and pigs are naturally susceptible; sheep and goats are rarely affected.

83 Etiology

VS is caused by a *Vesiculovirus* in the family Rhaboviridae. The virion is a large, bullet-shaped (65- to 185-nm) RNA virus. There are two major immunological types of VS virus (VSV): New Jersey and Indiana. The serotype Indiana is further categorized into three subtypes: Indiana 1, Indiana 2 (Cocal), and Indiana 3 (Alagoas). In addition to these two serotypes of VSV, there are other viruses within the genus *Vesiculovirus* that experimentally can cause vesicular lesions in domestic animals and infect humans:

- Piry—first isolated from an opossum in Brazil
- Chandipura—first isolated from a person in India
- Isfahan—isolated from sandflies and humans in Iran

84 Electron micrograph of VSV from an outbreak in Colorado.

85 History

A vesicular disease apparently affected horses in the Civil War, but VS was first recognized as disease entity in 1916. VS appeared and caused considerable problems in Midwest collection centers for horses used in World War I. The disease spread to eastern shipping ports and to France but died out in Europe. VS now occurs only in the Western Hemisphere.

Host Range

86 VSV has been shown to infect a wide number of hosts. In decreasing order of severity of infection, hosts include horses, donkeys, mules, cattle, swine, and humans. Wild animal hosts include deer, raccoons, bobcats, and monkeys.

South American camelids can develop clinical infection.

Sheep and goats are quite resistant and are rarely affected.

Geographic Distribution

87 Classical VS occurs only in the North America, Central America, and the northern part of South America. Serotypes New Jersey and Indiana 1 occur in the United States and Central America. Serotypes New Jersey and Indiana 1, 2, and 3 occur in South America.

Transmission

88 VSV has been shown to be transmitted by the sand fly and the black fly. Transovarial transmission has been shown to occur in both these flies. Before the 1982 VS outbreak in the United States, people expected an outbreak to stop about 2 weeks after a killing frost. In the 1982 outbreak, cases developed and the disease spread throughout the winter. The winter spread of the disease is believed to have resulted from exposure of cattle to contaminated waterers and feed bunks, as well as contact with infected animals. It is known that VSV can be spread by a contaminated milking machine. Overwintering did not occur in the 1995 outbreak in the United States.

Humans may be infected by contact and by aerosol.

Epidemiology

89 VS occurs throughout the year in subtropical and tropical areas of the Americas and sporadically during the warm months in the Southern and Western United States. Epidemics occur at roughly 10-year intervals. VS

is spread by insect vectors and movement of infected animals. Researchers at the University of Georgia have shown transovarial transmission in the sand fly; this may be a way the virus can overwinter.

Incubation Period

90 The incubation period for VS is similar to that for FMD. After intradermal lingual inoculation of VSV, a vesicle appears in about 24 hours.

In humans, the incubation period is 24 to 48 hours.

Pathogenesis

91 The animals develop a fever, and VSV may spread from the site of inoculation to sites of predilection for lesions, but viremia has not been detected. Experimental cases can be created only by intradermal–lingual inoculation.

Clinical Signs of VS

Animals develop a fever of 104 to 106 °F (40 to 41 °C).

In Horses

Vesicles in the mouth may cause a horse to champ its jaws, drool, and/or rub its mouth on the manger or other objects. Lesions on the coronary band can cause lameness.

92 Erosions and exudate in the nares.

93 Erosions and exudate at the mucocutaneous junction of the lips.

94 Erosions—ruptured vesicles—of the gingiva.

95 Erosions—ruptured vesicles—on the tongue.

96 Erosions—ruptured vesicles—on the tongue.

97 Erosions and dried exudate on the coronary band.

98 Erosions and dried exudate on the coronary band and heel.

In Cattle and Pigs

Clinical signs are very similar to those of FMD.

99 Series of slides showing the clinical signs of VS in cattle.

100 Cow drooling because of mouth lesions.

101 Erosions on the dental pad.

102 Erosions on the dental pad and gingiva.

103 Vesicles on the tongue.

104 Erosions on a teat.

105 Vesicles and erosions on the teats.

106 Hyperemia and beginning erosions on the coronary bands.

107 Hyperemia and erosions on the heels.

108 A large vesicle on the snout.

109 Ruptured vesicles on the snout.

110 Erosions on the lips and nares of a goat.

In Humans

VSV causes an influenzalike illness in people: symptoms include fever, headache, muscular aches, and blisters in the mouth similar to those caused by herpesvirus. The disease course lasts 4 to 7 days.

Microscopic Lesions

The histologic appearance of the vesicular lesion on the tongue is distinct from that seen in FMD. The cells in the affected area of stratum spinosum stain more deeply eosinophilic than normal, have a pycnotic nucleus, and are separated by an intercellular edema. However, in VS the cells do not become separated as they do in FMD but remain sufficiently attached to each other to form a lacelike or reticular pattern in the stratum spinosum.

111 Photomicrograph of a vesicle on the tongue of a cow.

Morbidity and Mortality

112 Interesting data on the economic effects of VS in cattle was collected by Dr. Fred Alderink during the 1982 outbreak of VS in Colorado. In 13 of the dairy herds studied, there were 2,404 cows and 378 cases of VS. In these 378 affected cows, lesions were distributed as follows:

Oral lesions only:	263 animals (69.3 percent)
Teat lesions only:	87 animals (23 percent)
Oral and teat lesions:	22 animals (5.8 percent)
Foot lesions only:	7 animals (1.9 percent)

Herds experiencing primarily oral lesions had an attack rate of 19.8 percent. The attack rate in two of four herds with teat lesions was 55.8 percent, and in the other two herds was 1.6 percent. The clinical course in cases with oral lesions was 23.8 days. Mastitis complicated 72 percent of the cases with teat lesions.

The total cost to the 13 dairy herd owners was $95,752 for an average cost of $253 per case. The average cost of a VS case with oral lesions only was $174 while the cost of a case with teat lesions averaged $568. Of the total $95,752 loss, 46 percent was for cows culled, 30 percent was for decreased production, 11 percent was for deaths, and 11 percent was for drugs, labor, weight loss, and veterinary charges.

Differences Between VS and FMD

113 Characteristics of VS that differentiate it from FMD are these:

- Horses are affected.
- There is sporadic incidence in the herd.
- A small percentage of animals have lesions at more than one site of predilection.
- There are no rumen lesions.
- There are no heart lesions.
- VS is less severe in young animals.
- Stabled animals usually are not affected by VS.

In spite of these differences, one should not attempt to make a final differential diagnosis in the field. Laboratory confirmation of the diagnosis is essential.

Diagnosis

114 In cattle, VS should be considered whenever salivation and lameness occur simultaneously and/or a vesicular lesion is seen or suspected. Early diagnostic lesions may be found before animals start to salivate, have nasal discharge, or become lame. To avoid missing a diagnosis, examine the mouth of a lame animal and the feet of any animal with signs or lesions involving the mouth or nostrils. Remember that in areas where VS is endemic, the disease can occur sporadically in individual animals in a herd or in many animals at once.

In pigs, sheep, and goats, you should consider VS when animals have sore feet and/or you suspect a vesicular lesion.

Specimens for Laboratory Diagnosis

Because the various vesicular diseases have similar clinical signs, a laboratory diagnosis for VS is mandatory. Oral, nasal, podal, or mammary lesions are good sources of specimens. The following should be collected from each of two or three animals:

1. Vesicular fluid—as much as possible.

2. Epithelium covering a vesicle.

3. Flaps of epithelial tissue still attached.

For 2 and 3 above, try to collect about 0.5 g. Old necrotic or fibrinous material that is difficult to remove is undesirable and often is highly contaminated with bacteria.

4. About 5 mL of blood with anticoagulant. Viremia ends about 5 days after the onset of disease.

5. Esophageal–pharyngeal (OP) fluid from convalescent cattle, sheep, or goats—about 5 mL. This should be immediately diluted with an equal volume of cell culture fluid (e.g., Hanks balanced salt solution with lactalbumin hydrolysate) and shaken vigorously for about 1 minute. If the solution turns yellow (indicating a low pH that could inactivate the virus), discard it and collect another sample.

6. Blood for serum (10 mL of serum)

If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quick-freeze the specimens and do not allow them to thaw during transit. If dry ice is used, be sure that the vials are tightly sealed with stopper and tape so that no carbon dioxide enters the vial. The carbon dioxide will lower the pH and inactive FMDV. Epithelium can also be placed in buffered glycerin and kept at 39 °F (4 °C) or –4 °F (–20 °C). The ratio of epithelium to glycerin should not exceed 1:10.

Control

115 Steps in a VS control program are these:

- Control movement of animals. Do not allow movement from an infected premises, except for slaughter, for 30 days after the last lesion has healed.
- Separate infected and healthy animals.
- Stable animals if possible.
- Disinfect milking machines between cows.
- Milk VS-infected cows last.
- Control insects.

Vaccination

Commercial vaccine for VS is available.

116 Swine Vesicular Disease (SVD)

Definition

117 SVD is an acute, contagious viral disease of swine caused by an enterovirus and characterized by fever and vesicles with subsequent erosions in the mouth and on the snout, feet, and teats.

Etiology

118 SVD virus (SVDV) is in the enterovirus group of picornaviruses. SVDV is closely related to the human enterovirus Coxsackie B–5 and unrelated to known porcine enteroviruses. Some researchers say that this is a case where a human pathogen went into pigs when they came into contact with human excretions. The virion is a roughly spherical, 28-nm single-stranded RNA virus. SVDV is resistant over a wide pH range (2.5 to 12) and relatively resistant to heat (inactivated at 157 °F [69 °C]). It persists for a long time—up to 2 years—in salted, dried, or smoked meat products.

Disinfectants

119 Disinfectants include 10-percent formalin, 70-percent alcohol, 2-percent sodium hydroxide (pH 12.4), 1.5-percent bleach (5.25-percent sodium hypochlorite), and some of the newer iodophore and chlorine dioxide disinfectants.

History

120 SVD was first described in Italy in 1966. The second report came from Hong Kong in 1971, when the disease occurred during an FMD vaccine trial. SVD was first thought to be due to an FMD virus (FMDV) variant, but the isolate was then shown to be not FMDV but a relative of the agent that caused the 1966 outbreak in Italy. Since 1966, SVD has occurred in many European countries. In the early 1990's, there were outbreaks in Italy, Spain, and Portugal.

Host Range

121 SVD affects pigs. Laboratory infections can be induced in humans and baby mice.

Geographic Distribution

122 SVD has occurred in Italy, Hong Kong, England, Scotland, Wales, Japan, Malta, Austria, Belgium, France, the Netherlands, Germany, Poland, Switzerland, Greece, and Spain. The 1990's outbreaks occurred in Italy, Spain, and Portugal.

Transmission

123 SVD is transmitted by direct or indirect contact with infected feces, as well as by feeding pigs contaminated garbage.

Epidemiology

SVD can be introduced into a herd of pigs by feeding garbage containing infected meat scraps, by introducing infected animals, or by allowing pigs to contact feces from infected animals (e.g., by shipping pigs in an improperly cleaned truck). From recent outbreaks in Europe, it appears that the SVD-infected animals introduced into a herd may show no clinical sign of the disease, indicating that there is a subclinical form of SVD. After initial infection, the disease spreads through contact of susceptible pigs with infected pigs or feces from infected pigs.

Incubation Period

124 Signs of SVD develop in 2 to 3 days after eating contaminated food and in 2 to 7 days after contact with infected pigs.

Pathogenesis

After infection, pigs develop viremia. The virus is shed primarily in the feces. Tissues from pigs killed during the viremic period contain up to 10 million infectious particles per gram. In experiments with hams produced by the Spanish dry-cure process, SVDV persisted in lymph nodes for almost 2 years.

Clinical Signs

125 The clinical signs of SVD include

- Fever
- Vesicles in the mouth and on the snout and feet—grossly indistinguishable from those caused by FMD
- Unsteady gait, shivering, and chorea (jerking) type leg movements due to an encephalitis
- Lameness

Gross Lesions

Vesicles caused by SVD are indistinguishable from those caused by FMD.

126 Vesicle on the snout.

127 Ruptured vesicle on the snout.

128 "Dry" type lesions on the surface of the tongue.

129 Ruptured vesicles in the area of the coronary bands of the claws and dewclaws.

130 Ruptured vesicles on the heels.

131 Ruptured vesicles on the heel of the claw and above the dewclaws.

132 Old—no tags of tissue and smooth—vesicles on a teat.

Microscopic Lesions

A nonsuppurative cuffing of blood vessels in the brain.

133 Photomicrograph of the nonsuppurative encephalitis that can occur in an SVD infection.

Morbidity and Mortality

134 There is lower morbidity with SVD than with FMD. Lesions in SVD are less severe than lesions in FMD. Essentially, there is no mortality associated with SVD.

Diagnosis

135 In pigs, SVD should be considered whenever there is lameness and/or vesicles on the coronary bands, soles of the feet, interdigital spaces, tongue, nares, and/or lips. Fever often precedes other clinical signs; therefore, febrile animals should be carefully examined. To avoid missing a diagnosis, examine the mouth of a lame pig and the feet of any pig with signs of lesions involving the mouth or nostrils. Remember that there are mild and subclinical forms of SVD that may go undetected unless a careful examination is made.

Specimens for Laboratory Diagnosis

Because the various vesicular diseases have similar clinical signs, a laboratory diagnosis for SVD is mandatory. Oral, nasal, podal, or mammary lesions are good sources of specimens. The following should be collected from each of two or three animals:

1. Vesicular fluid—as much as possible.

2. Epithelium covering a vesicle.

3. Flaps of epithelial tissue still attached.

For 2 and 3 above, try to collect about 0.5 g. Old necrotic or fibrinous material that is difficult to remove is undesirable and often is highly contaminated with bacteria.

4. About 5 mL of blood with anticoagulant. Viremia ends about 5 days after the onset of disease.

5. Blood for serum (10 mL of serum)

If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quick-freeze the specimens and do not allow them to thaw during transit. If dry ice is used, be sure that the vials are tightly sealed with stopper and tape so that no carbon dioxide enters the vial.

Serology is complicated by cross-reactions with other undefined porcine enteroviruses.

Control

Prevention measures for SVD are similar to those for FMD:

136

- Control of animals imported from infected areas
- Sanitary disposal of garbage from international aircraft and ships

Vaccination

There is no SVD vaccine.

Eradication Measures

Several measures can be taken to eradicate SVD:

137

- Quarantine of infected farms and areas
- Slaughter and disposal of infected and contact pigs
- Cleaning and disinfection of infected premises

138 Vesicular Exanthema of Swine (VES)

Definition

139 VES is an acute, febrile disease of swine caused by caliciviruses and characterized by fever and vesicles with subsequent erosions in the mouth and on the snout, feet, and teats.

Etiology

140 VES is caused by a calicivirus. There are 13 serotypes of VES virus (VESV). VESV's are closely related to at least 14 serotypes of calicivirus in the San Miquel sea lion virus group.

141 Electron photomicrograph of VESV. Notice the cuplike cavities on the surface of the virions.

142 History

1932	A vesicular disease in swine in Buena Park, CA, thought to be FMD: 19,000 pigs are killed and buried.
1933	A vesicular disease in swine in San Diego County is shown not to be FMD, and the disease is named vesicular exanthema of swine.
1932–36	Ten more outbreaks of VES occur in California, and each is eradicated.
1936–39	There is no VES outbreak.
1939–52	VES spreads to all the major swine-producing areas in the United States. It is believed to have spread from California though garbage carried on a train running between California and Chicago, and by getting into a hog-cholera antiserum production plant in North Platte, NE.
1954	National VES eradication program is started.

1954	A law is enacted requiring that garbage fed to pigs be cooked.
1956	The last case of VES is recorded.
1959	The United States is declared free of VES, and VES is declared a foreign disease.
1972	The existence of marine calicivirus is recognized.
1972–95	At least 14 marine caliciviruses are recognized; it is likely that all can experimentally produce vesicles in pigs.

During the period that VES occurred in the United States, there was an outbreak in pigs aboard a ship bound for Honolulu; the pigs were killed. There was also an outbreak in Iceland, which probably resulted from feeding pigs garbage containing U.S. pork scraps.

People have speculated that VES may have resulted from feeding of marine mammal (seal) meat and fish as a protein supplement during the Great Depression. Thus, some are concerned that a VES-like disease could reappear in the United States because of the large number of marine mammals on the West Coast. Marine calicivirus antibody has not yet been found in marine mammals in the Atlantic Ocean.

Host Range

143 VES occurs in pigs. Related caliciviruses occur in marine mammals and fish in the Pacific Ocean.

Geographic Distribution

144 VES has been eradicated.

Transmission

145 VES is transmitted by direct and indirect contact with infected pigs, as well as by infected pork products in uncooked garbage.

Epidemiology

146 VES outbreaks up to 1939 may have been due to separate introductions of the virus. Starting in the 1939 outbreak, there was rapid pig-to-pig spread and spread via infected pork scraps in uncooked garbage.

Incubation Period

147 The VES incubation period is 18 to 72 hours after natural exposure.

Clinical Signs

148 The clinical signs of VES are these:

- Fever
- Lesions clinically indistinguishable from those caused by FMD
- Lameness
- Lesions seem to be deeper than in other vesicular diseases, and granulation tissue commonly forms, especially on the feet.

Gross Lesions

Vesicles in VES are indistinguishable from those in FMD.

149 Large vesicle on the snout.

150 Ruptured vesicles on the snout.

151 Blanching of the coronary band; hyperemia above the band.

152 Blanching of the coronary band; ruptured vesicle on the coronary band.

153 Old VES lesions on the heels and dewclaws.

154 Ruptured vesicle at the base of the teat.

155 Ruptured vesicle caused by a virus of the San Miquel sea lion virus group on the flipper of a seal.

156 Ruptured vesicle on the heals of a pig experimentally inoculated with a virus of the Miquel sea lion virus group.

Morbidity and Mortality

157 Morbidity from VES is quite variable but may be near 100 percent. Mortality from VES is low.

Diagnosis

158 In pigs, VES should be considered whenever there is lameness and/or vesicles on the coronary bands, soles of the feet, interdigital spaces, tongue, nares, and/or lips. Fever often precedes other clinical signs; therefore, febrile animals should be carefully examined. To avoid missing a diagnosis, examine the mouth of a lame pig and the feet of any pig with signs of lesions involving the mouth or nostrils.

Specimens for Laboratory Diagnosis

Because the various vesicular diseases have similar clinical signs, a laboratory diagnosis for VES is mandatory. Oral, nasal, podal, or mammary lesions are good sources of specimens. The following should be collected from each of two or three animals:

1. Vesicular fluid—as much as possible.

2. Epithelium covering a vesicle.

3. Flaps of epithelial tissue still attached.

For 2 and 3 above, try to collect about 0.5 g. Old necrotic or fibrinous material that is difficult to remove is undesirable and often is highly contaminated with bacteria.

4. About 5 mL of blood with anticoagulant. Viremia ends about 5 days after the onset of disease.

5. Blood for serum (10 mL of serum).

If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quick-freeze the specimens and do not allow them to thaw during transit. If dry ice is used, be sure that the vials are tightly sealed with stopper and tape so that no carbon dioxide enters the vial.

Control

159 The control of VES requires slaughter and disposal.